

have amended the title of the present application to remove the term "novel". In compliance with 37 C.F.R. § 1.121(b)(1)(iii), a marked up copy of the original title is attached hereto as **Exhibit C**.

Applicants request that, since the objection has been overcome, this objection be withdrawn.

IV. Rejection of Claims 1 and 5-9 Under 35 U.S.C. § 101

The Action first rejects claims 1 and 5-9 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

The present invention has a number of substantial and credible utilities, not the least of which is in diagnostic assays, as described in the specification, at least at page 10, lines 27-33. As described in the specification from page 15, line 33 through page 16, line 32, the present sequence defines several coding single nucleotide polymorphisms - specifically, an A/G transition at nucleotide position 271 of SEQ ID NO:6, which can result in an asparagine or glutamate being present at corresponding amino acid position 91 of SEQ ID NO:7; a C/G transversion at nucleotide position 364 of SEQ ID NO:6, which can result in an arginine or glycine being present at corresponding amino acid position 122 of SEQ ID NO:7; a G/A transition at nucleotide position 367 of SEQ ID NO:6, which can result in a glycine or serine being present at corresponding amino acid position 123 of SEQ ID NO:7; a T/A transversion at nucleotide position 699 of SEQ ID NO:6, which can result in a serine or asparagine being present at corresponding amino acid position 233 of SEQ ID NO:7; a T/C transition at nucleotide position 1013 of SEQ ID NO:6, which can result in an isoleucine or threonine being present at corresponding amino acid position 338 of SEQ ID NO:7; a G/A transition at nucleotide position 1015 of SEQ ID NO:6, which can result in a valine or methionine being present at corresponding amino acid position 339 of SEQ ID NO:7; a C/A transversion at nucleotide position 1397 of SEQ ID NO:6, which can result in a proline or histidine being present at corresponding amino acid position 466 of SEQ ID NO:7; a G/C transversion at nucleotide position 1405 of SEQ ID NO:6, which can result in an aspartate or histidine being present at corresponding amino acid position 469 of SEQ ID NO:7; and a G/T transition at nucleotide position 1419 of SEQ ID NO:6, which can result in a glutamate or aspartate being present at corresponding amino acid position 473 of SEQ ID NO:7. As such polymorphisms are the basis for diagnostic assays such as forensic analysis, which does **not** require the identification of a specific medical condition, and is undoubtedly a "real world" utility, the present

sequences must in themselves be useful. It is important to note that the presence of more useful polymorphic markers for forensic analysis would not mean that the present sequences lack utility. As clearly set forth by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Just because other polymorphic sequences from the human genome have been described does not mean that the use of the presently described polymorphic markers for forensic analysis is not a specific utility.

The Examiner states that the specification does not "disclose the biological role" for the claimed sequences (Action at page 2). Applicants disagree, as the presently claimed sequence is clearly referred to as an ion channel protein (see, at least, the specification at page 1, lines 9-12, and page 2, lines 5-7), and further, that such ion channel proteins "mediate or facilitate the passage of materials across the lipid bilayer" (specification at page 1, lines 26-27). Furthermore, Applicants would like to invite the Examiner's attention to the fact a sequence sharing nearly 100% percent identity at the protein level over extended portions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as "Homo sapiens two-pore calcium channel protein 2" (GenBank accession number AY029200; GenBank report and alignment shown in **Exhibit D**). The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation, there can be no question that those skilled in the art would clearly believe that Applicants' sequence is an ion channel protein.

The Action cites an article by Doerks *et al.* (Trends in Genetics 14:248-250, 1998) for the proposition that sequence-to-function methods of assigning protein function are prone to errors. However, Doerks *et al.* states that "utilization of family information and thus a more detailed characterization" should lead to "simplification of update procedures for the entire families if functional

information becomes available for at least one member” (Doerks *et al.*, page 248, paragraph bridging columns 1 and 2, emphasis added). Applicants point out that, as detailed above, a sequence sharing nearly 100% percent identity at the protein level over extended regions of the claimed sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as a two-pore calcium channel protein (see **Exhibit D**). The two-pore ion channel superfamily is a well-studied protein family with a large amount of known functional information, exactly the situation that Doerks *et al.* suggests will “simplify” and “avoid the pitfalls” of previous sequence-to-function methods of assigning protein function (Doerks *et al.*, page 248, columns 1 and 2). Thus, instead of supporting the Examiner’s position against utility, Doerks *et al.* actually supports Applicants’ position that the presently claimed sequences have a substantial and credible utility.

The Examiner next cites Brenner (TIG 15:132-133, 1999) as teaching that “most homologs must have different molecular and cellular functions” (Action at page 5). However, this statement is based on the assumption that “if there are only 1000 superfamilies in nature, then most homologs must have different molecular and cellular functions” (Brenner, page 132, second column). Furthermore, Brenner suggests that one of the main problems in using homology to predict function is “an issue solvable by appropriate use of modern and accurate sequence comparison procedures” (Brenner, page 132, second column), and in fact references an article by Altschul *et al.*, which is the basis for one of the “modern and accurate sequence comparison procedures” used by Applicants. Thus, the Brenner article also does not support the alleged lack of utility.

The Examiner finally cites Bork *et al.* (Trends in Genetics 12:425-427, 1996) as supporting the proposition that prediction of protein function from homology information is somewhat unpredictable, based on the “structural similarity of a small domain of the new protein to a small domain of a known protein” (Action at page 5). Thus, the Examiner’s reliance on Bork *et al.* has the same failing as described above for Doerks *et al.*, specifically, the assumption that Applicants assertion that the present sequence is an ion channel protein is made on the basis of structural similarity of a small domain of the new protein to a small domain of a known protein. Applicants again would like to invite the Examiner’s attention to the fact a sequence sharing nearly 100% percent identity at the protein level over extended regions of the claimed sequence is present in the leading scientific repository for

biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as a two-pore calcium channel protein (see **Exhibit D**). Thus, Applicants assertion that the present sequence is an ion channel protein is not made on the basis of "structural similarity of a small domain of the new protein to a small domain of a known protein", but rather vast homology over large tracts of the sequence. Thus, Bork *et al.* also does not support the alleged lack of utility for the present invention.

Rather, as set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable (*State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

In *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between

35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. The Examiner implies that a “real-world” utility does not require “further characterization” (Action at page 3). However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit’s holding in *Brana*, which clearly states, as highlighted in the quote above, that “pharmaceutical inventions, necessarily includes the expectation of further research and development” (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is “undue”, not “experimentation”. *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra; Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

As an additional example of the utility of the present nucleotide sequences, the specification details on page 5, lines 35-37, that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such “DNA chips” clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. As the present sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Given the widespread utility of such “gene chip” methods using *public domain* gene

sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Evidence of the “real world” substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, two such companies (Agilent acquired by American Home Products and Rosetta acquired by Merck) were viewed to have such “real world” value that they were acquired by large pharmaceutical companies for significant sums of money. The “real world” substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, *Science* 291:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, *Science* 291:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, as described in the specification at least from page 2, line 36 to page 3, line 2, the present nucleotide sequences have a specific utility in “identification of coding sequence” and “mapping a unique gene to a particular chromosome”. This is evidenced by the fact that SEQ ID NO:6 can be used to map the 15 coding exons on chromosome 11 (present within the chromosome 11 clone

presented in Genbank Accession Number AP003071; alignment and the first page from the Genbank report are presented in **Exhibit E**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 11 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Applicants respectfully remind the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence, as described above. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The specification details that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics" (specification from page 10, line 33 to page 11, line 2). Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (*supra* at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the

requirements of 35 U.S.C. § 101.

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office (“the PTO”) itself for compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the “real-world” utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section V, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1 and 5-9 under 35 U.S.C. § 101 has been overcome, and request that the rejection

be withdrawn.

V. Rejection of Claims 1 and 5-9 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1 and 5-9 have been shown to have "a specific, substantial, and credible utility", as detailed in section IV above, the present rejection of claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1 and 5-9 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Rejection of Claim 5 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claim 5 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for "hybridization" (Action at page 5). Applicants respectfully traverse.

The Action states that the specification "does not reasonably provide enablement for a nucleic acid which (*sic*) hybridizes to SEQ ID NO:6" (Action at page 5). The Examiner seems to take this position because "insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which (*sic*) will retain the characteristics" of the claimed sequence (Action at page 5). Applicants point out that the above comment is completely irrelevant to determining whether the claimed compositions meet the legal requirements for patentability under 35 U.S.C. § 112, first paragraph. There is absolutely no requirement that all species of an invention must have all of the exact same properties. It is well established that the enablement requirement is met if any use of the invention (or in this case, certain species of the invention) is provided (*In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka*, *supra*). "The enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), citing *Engel Indus., Inc. v. Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991). The Examiner has already conceded that SEQ ID NO:6 is enabled. Thus, the enablement

issue should be resolved. Enablement only requires that the specification describe a practical use for the composition defined in the claims, and that a skilled artisan be able to make and use the claimed DNA segments without undue experimentation. Accordingly, by the Examiner's own admission, the § 112 requirement has certainly been met.

The Action seems to contend that the specification provides insufficient guidance regarding the biological function or activity of certain of the claimed compositions. However, such an enablement standard conflicts with established patent law. As discussed *In re Brana, supra*, the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442.

The Examiner states that the present invention could not be practiced without "undue experimentation" (Action at page 5). However, it is important to remember that in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin, supra*. In *In re Wands, supra*, the P.T.O. took the position that the applicant failed to demonstrate that the disclosed biological processes of immunization and antibody selection could reproducibly result in a useful biological product (antibodies from hybridomas) within the scope of the claims. In its decision overturning the P.T.O.'s rejection, the Federal Circuit found that Wands' demonstration of success in four out of nine cell lines screened was sufficient to support a conclusion of enablement. The court emphasized that the need for some experimentation requiring, *e.g.*, production of the biological material followed by routine screening, was not a basis for a finding of non-enablement, stating:

Disclosure in application for the immunoassay method patent does not fail to meet enablement requirement of 35 USC 112 by requiring 'undue experimentation,' even though production of monoclonal antibodies necessary to practice invention first requires production and screening of numerous antibody producing cells or 'hybridomas,' since practitioners of art are prepared to screen negative hybridomas in order to find those that produce desired antibodies, since in monoclonal antibody art one 'experiment' is not simply screening of one hybridoma but rather is entire attempt to make desired antibody, and since record indicates that amount of effort needed to obtain desired antibodies is not excessive, in view of Applicants' success in each attempt to produce antibody that satisfied all claim limitations.

Wands at 1400. Thus, the need for some experimentation does not render the claimed invention

unpatentable under 35 U.S.C. § 112, first paragraph. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., supra*.

Applicants point out that significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling to chromosomal mapping are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

The Action questions the teaching and guidance in the specification for certain aspects of the present invention. However, as discussed above, this requirement is completely misplaced. The specification provides ample teaching regarding the various hybridization conditions that can be employed in various aspects of the invention, for example at page 4, lines 23-32. Thus, the skilled artisan can readily make and use the claimed invention.

Furthermore, there is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design a hybridization experiment. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.* (*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought

to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi & Horton, 169 USPQ 367, 369 (CCPA 1971), emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra*. In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques such as nucleic acid hybridization techniques are routine in the art, such protocols do not need to be described in detail in the specification.

Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. The present claims are thus enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

As detailed above, all aspects of the enablement rejection under 35 U.S.C. § 112, first paragraph have been overcome. Applicants therefore respectfully request that the rejection be withdrawn.

VII. Rejection of Claim 5 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claim 5 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*." *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable

clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the . . . nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

In claims to genetic material . . . a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition.

It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself*.

Using the nucleic acid and amino acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to distinguish the claimed nucleic acids from other materials on the basis of the specific structural description provided. Polynucleotides that encode SEQ ID NO:7 and hybridize to SEQ ID NO:6 or the complement thereof under specific highly stringent hybridization conditions, are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. Claim 5 thus meets the written description requirement.

For each of the foregoing reasons, Applicants submit that the rejection of claim 5 under 35 U.S.C. § 112, first paragraph, has been overcome, and request that the rejection be withdrawn.

VIII. Rejection of Claim 5 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claim 5 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action rejects claim 5 as allegedly indefinite based on the term "highly stringent hybridization conditions", because the specific hybridization and washing conditions are not recited in the claim. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). However, while Applicants submit that the term is sufficiently definite, as a number of highly stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to recite specific highly stringent hybridization conditions. As the specification provides specific teaching regarding highly stringent hybridization conditions, at least at page 4, lines 24-35, Applicants submit that revised claim 5 even more clearly meets the requirements of 35 U.S.C. § 112, second

paragraph.

Applicants therefore respectfully request withdrawal of this rejection.

IX. Rejection of Claim 5 Under 35 U.S.C. § 102(b)

The Action next rejects claim 1 under 35 U.S.C. § 102(b), as allegedly anticipated by Adams *et al.* (Genbank accession number AA309878; "Adams"). Applicants respectfully traverse.

Applicants respectfully point out that claim 5 requires the isolated nucleic acid molecule both to hybridize to the nucleotide sequence of SEQ ID NO:6 or the complement thereof under highly stringent conditions **and** to encode the amino acid sequence of SEQ ID NO:7. Applicants submit that, as admitted in the Action, an isolated nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO:7 is neither taught nor suggested by Adams, the present rejection of claim 5 under 35 U.S.C. § 102(b) is improper, and should be withdrawn.

Applicants submit that the rejection of claim 5 under 35 U.S.C. § 102(b) has been overcome, and respectfully request withdrawal of the rejection.

X. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Murphy have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

March 12, 2003

Date

David W. Hibler

David W. Hibler
Agent for Applicants

Reg. No. 41,071

LEXICON GENETICS INCORPORATED
8800 Technology Forest Place
The Woodlands, TX 77381
(281) 863-3399

Exhibit B

Marked Up Version of Amended Claims in U.S. Patent Application Ser. No. 09/918,359

1. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:7.

5. (Twice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

- (a) encodes the amino acid sequence of SEQ ID NO:7; and
- (b) hybridizes [under highly stringent conditions] to the nucleotide sequence of SEQ ID NO:6 or the complement thereof under highly stringent conditions of 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

6. (Amended) An isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO:6.

7. A recombinant expression vector comprising the isolated nucleic acid molecule of claim 1.

8. The recombinant expression vector of claim 7, wherein said isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:6.

9. A host cell comprising the recombinant expression vector of claim 7.

Exhibit C

Marked Up Version of Amended Title in U.S. Patent Application Ser. No. 09/918,359

[Novel] Human Ion Channel Proteins and Polynucleotides Encoding the Same

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Identities = 123/123 (100%)
Strand = Plus / Plus

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Query: 540 cactactactttgactacctggggaacctcatcgccctggcaaacctgggtgtccatttgc 599
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Sbjct: 93047 cactactactttgactacctggggaacctcatcgccctggcaaacctgggtgtccatttgc 93106

Query: 600 gtg 602
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Sbjct: 93107 gtg 93109

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Strand = Plus / Plus

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Query: 438 cctatcctccatgggtgggggaggaggagccttcctcaggc 479
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Strand = Plus / Plus

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Query: 848 tcatcggttccgcttctgcgtatcatccccagcatgaag 888
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Strand = Plus / Plus

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Query: 1343 aggccacctaccagatgactgtggagctcctgttcagg 1380
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Strand = Plus / Plus

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Score = 170 bits (86), Expect = 2e-39
Identities = 86/86 (100%)
Strand = Plus / Plus

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Strand = Plus / Plus

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Strand = Plus / Plus

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Strand = Plus / Plus

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WRPEMVGLLSLWDMTRMLNMLIVFRFLRIIPSMKPMVAVASTVLGLVQNMRAFGGILVVV
Sbjct: 1689 WRPEMVGLLSLWDMTRMLNMLIVFRFLRIIPSMKPMVAVASTVLGLVQNMRAFGGILVVV 1868

Query: 323 YYVFAIIGINLFRGVIVALPGNSSAPANGSAPCGSFEQLEYWANNFDDFAAALVTLWNL 382
YYVFAIIGINLFRGVIVALPGNSSAPANGSAPCGSFEQLEYWANNFDDFAAALVTLWNL
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Query: 443 LAGTPEATYQMTVELLFRDILEEPGEDELTERLSQHPhlWLCR 485
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TRRG PSTSLRFCRAPSSSSATTTLTWTGTSPPWQTWCPFACSWCWMQMCCLLSVMTSSWG
Sbjct: 1329 TRRG PSTSLRFCRAPSSSSATTTLTWTGTSPPWQTWCPFACSWCWMQMCCLLSVMTSSWG 1508

Query: 221 FSTASSLCTTCWSCCSRSLPWACEGTCPTPATCLTGSSPLSCW 263
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Identities = 113/114 (99%), Positives = 114/114 (100%)
Frame = +3

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+QQDDGQDRERLTYFQNLPESLTSLLVLLTTANNPDVMIPAYSKNRAYAIFVFTVIGSL
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Query: 108 FLMNLLTAIIYSQFRGYLMKSLQTSIFRRRLGTAAFEVLSSMVGEAGFPQA 160
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cds
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Frame = +3

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WRPEMVGLLSLWDMTRMLNMLIVFRFLRIIPSMKPMVAVASTVLGLVQNMRAFGGILVVV
Sbjct: 1689 WRPEMVGLLSLWDMTRMLNMLIVFRFLRIIPSMKPMVAVASTVLGLVQNMRAFGGILVVV 1868

Query: 323 YYVFAIIGINLFRGVIVALPGNSSLAPANGSAPCGSFEQLEYWANNFDDFAAALVTLWNL 382
YYVFAIIGINLFRGVIVALPGNSSLAPANGSAPCGSFEQLEYWANNFDDFAAALVTLWNL
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Query: 383 MVVNNWQVFLDAYRRYS GPWSKIYFVLWWLVSSVIWVNLFLALILENFLHKWDPRSHLQP 442
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Query: 443 LAGTPEATYQMTVELLFRDILEEPGEDELTERLSQHPhlWLCR 485
LAGTPEATYQMTVELLFRDILEEP EDELTERLSQHPhlWLCR
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Identities = 102/103 (99%), Positives = 102/103 (99%)
Frame = +1

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Sbjct: 1329 TRRG PSTSLRFCRAPSSSSATTTLTWGTSSPWQTWCPFACSWCWMQMCCLLSVMTSSWG 1508

Query: 221 FSTASSLCTTCWSCCSRSLPWACEGTCPTPATCLTGSSPLSCW 263
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Identities = 113/114 (99%), Positives = 114/114 (100%)
Frame = +3

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Sbjct: 825 QQDDGQDRERLTYFQNLPESLTSLLVLLTTANNPDVMI PAYSKNRAYAIF FIVFTVIGSL 1004

Query: 108 FLMNLLTAIIYSQFRGYLMKSLQTS LFRRLGTAAFEVLSSMVGE GGAFFQA 160
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Identities = 130/131 (99%)
Strand = Plus / Plus

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Score = 244 bits (123), Expect = 1e-61
Identities = 123/123 (100%)
Strand = Plus / Plus

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Query: 540 cactactactttgactacctggggaacctcatcgccctggcaaacctgggtgtccatttgc 599
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Identities = 102/102 (100%)
Strand = Plus / Plus

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Score = 200 bits (101), Expect = 2e-48
Identities = 101/101 (100%)
Strand = Plus / Plus

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Score = 194 bits (98), Expect = 1e-46
Identities = 98/98 (100%)
Strand = Plus / Plus

Query: 1283 agaacttccttcacaagtgggacccccgcagccacctgcagccccttgctgggaccccag 1342
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Identities = 87/87 (100%)
Strand = Plus / Plus

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Query: 1179 tgcatatcggcgctactcaggcccggtg 1205
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Sbjct: 100401 tgcatatcggcgctactcaggcccggtg 100427

Score = 170 bits (86), Expect = 2e-39
Identities = 86/86 (100%)
Strand = Plus / Plus

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Query: 1095 ggccaacaacttcgatgactttgcgg 1120
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Sbjct: 100233 ggccaacaacttcgatgactttgcgg 100258

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Identities = 82/82 (100%)
Strand = Plus / Plus

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Query: 1437 gcacctgtggctgtgcaggtga 1458
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Score = 163 bits (82), Expect = 4e-37
Identities = 82/82 (100%)
Strand = Plus / Plus

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Identities = 78/78 (100%)
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Identities = 73/73 (100%)
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Score = 135 bits (68), Expect = 9e-29
Identities = 68/68 (100%)
Strand = Plus / Plus

Query: 247 gtgatgattcctgcgtattccaagaaccgggcctatgccatcttcttcatagtcttcact 306
|||||
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Score = 133 bits (67), Expect = 3e-28
Identities = 67/67 (100%)
Strand = Plus / Plus

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Score = 119 bits (60), Expect = 5e-24
Identities = 60/60 (100%)
Strand = Plus / Plus

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